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CLINICAL NOTE

Maxillary Malignant Mesenchymoma and Massive Fibrous Dysplasia

Matthew E. Beuerlein, MD; David E. Schuller, MD; Barry R. DeYoung, MD

This is the first report (to our knowledge) that describes a patient with massive polyostotic fibrous dysplasia involving the calvaria and facial skeleton that subsequently underwent transformation to a malignant mesenchymoma with elements of chondrosarcoma, osteosarcoma, and rhabdomyosarcoma arising in the maxilla. Malignant transformation occurred in the absence of prior radiation exposure, osteomyelitis, or known bony infarction. A review of the literature did not reveal any similar cases of massive fibrous dysplasia of the maxilla degenerating to multiple simultaneous malignant histotypes. *Arch Otolaryngol Head Neck Surg. 1997;123:106-109*

REPORT OF A CASE

A 29-year-old African American man with a history of polyostotic fibrous dysplasia since early childhood presented with a 1-month history of a rapidly enlarging bony lesion of the left maxilla (**Figure 1**). His medical history included hyperparathyroidism with hypercalcemia, bilateral nephrolithiasis, gout, pseudogout, depression, and a mixed hearing loss bilaterally. Fibrous dysplasia of the bony architecture had involved the calvaria, maxilla, mandible, ribs, vertebral column, pelvis, and proximal aspect of the femurs. Since childhood, the patient had undergone multiple surgical procedures that were undertaken to decrease the weight of, and sculpt, his massive craniofacial skeleton. The extent of deformity from the fibrous dysplasia had remained stable over the previous 5 to 7 years.

A biopsy was performed on the patient's left maxilla, which had rapidly enlarged, and the specimen was diagnosed as high-grade sarcoma. The patient was subsequently transferred to the Arthur G. James Cancer Hospital and Research Institute at The Ohio State University, Columbus, where findings of magnetic resonance imaging and computed tomography (**Figure 2**) confirmed the presence of a large mass with ill-defined borders involving the entire left maxilla. Treatment options were discussed with the patient, and informed consent was obtained. Surgery was undertaken soon thereafter because of the lesion's rapid growth rate. A left total maxillectomy with orbital preservation, along with intraoperative radiation therapy (10 Gy of 6 MeV was prescribed to the 90% isodose line), was performed. A midline hemifacial degloving approach was performed through a lateral rhinotomy and lower lip–dividing incision (**Figure 3**). The excised tumor weighed 1530 g and measured 23×18×15 cm. All clinically detectable tumor was removed before intraoperative radiation therapy was performed. The resulting maxillary defect was lined with split-thickness skin grafts with standard bolster support.

Histological examination showed a high-grade sarcomatous neoplasm that both eroded and expanded the maxilla. The tumor was variable in its appearance, with the majority of the lesion being composed of malignant cartilage characterized by increased cellularity, moderate nuclear atypia, and occasional mitotic figures. The average histological grade for the cartilage component of this lesion was grade II/III; however, areas of both well-differentiated chondrosarcoma and grade III tumor were present. Intimately admixed and blending with the neoplastic cartilage without sharp demarcation were foci of high-grade undifferentiated sarcoma. In some areas, the cells had a rhabdoid appearance with eccentrically placed oval nuclei and rather abundant eosinophilic cytoplasm. Other areas contained highly pleomorphic

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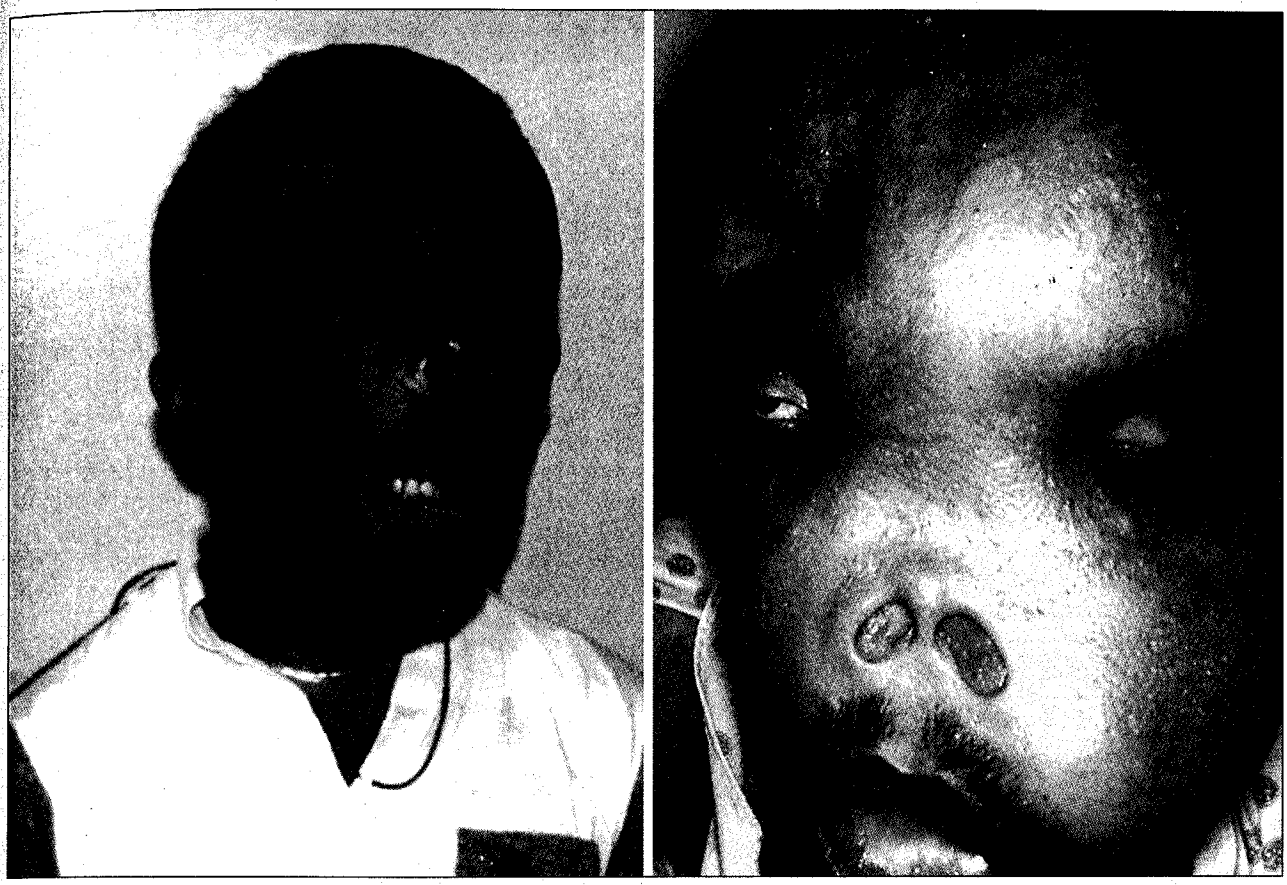

Figure 1. *Patient with polyostotic fibrous dysplasia including massive enlargement of the calvaria and facial bones. Note facial asymmetry due to left maxillary mass.*

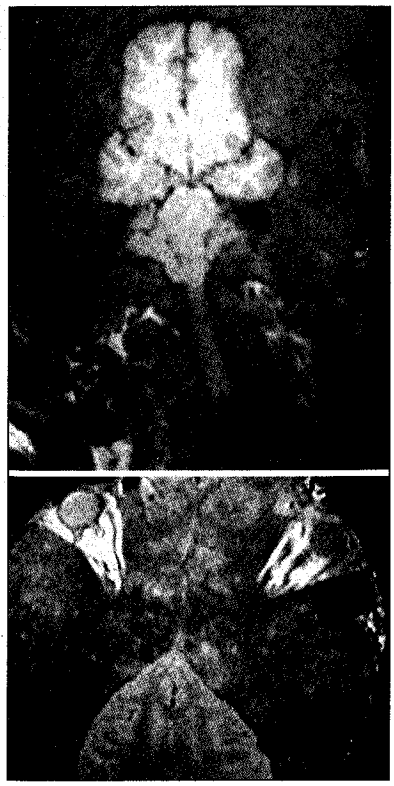

Figure 2. *Computed tomographic scan of the patient's head revealing massive calvarial enlargement, brain compression, and marked telecanthus.*

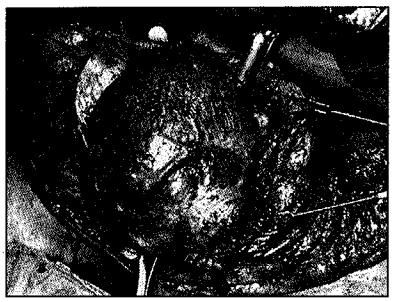

Figure 3. *Hemifacial degloving approach to maxillary tumor.*

cells separated by "lacy-appearing" eosinophilic material consistent with osteoid.

Immunohistochemical analysis showed the cartilaginous areas to be immunoreactive with antibodies directed against S100 protein, typical of this type of cell. The more high-grade, rhabdoid-appearing cells were decorated by anti–muscle-specific actin, indicative of muscle differentiation. The neoplasm arose in the background of conventional fibrous dysplasia characterized by irregular nonpurposeful bony trabeculae that appeared to arise from stromal cells. In some areas, the trabeculae were round, and in other areas, they appeared to form Chinese letter–type configurations.

The patient's postoperative course was uneventful, with the exception of 1 episode of paroxysmal supraventricular tachycardia in addition to gout and hypercalcemic pseudogout of an interphalangeal joint. The paroxysmal supraventricular tachycardia resolved spontaneously, and the joint inflammation responded rapidly to nonsteroidal anti-inflammatory therapy. The patient eventually was fitted with a massive maxillary prosthesis and began to take oral feedings on postoperative day 5 (**Figure 4**). Adjuvant therapy consisted of the previously described intraoperative radiation therapy followed by 4.5 Gy (25 fractions) of postoperative external beam radiation therapy to the left maxilla. The patient was to begin chemotherapy after completing the radiation therapy. At his 5-month follow-up visit, before he began chemotherapy, a 4×5-cm nodule was found at the medial aspect of the maxillary cavity, in addition to a soft mass at the site of a remote bicoronal incision on the right side of the scalp. Fine-needle aspirates from both lesions

were positive for osteosarcoma. Furthermore, a follow-up chest radiograph at this time was positive for a new finding of scattered bilateral pulmonary lesions. The patient died of metastatic disease 3 weeks later.

COMMENT

Fibrous or fibro-osseous dysplasia is a relatively common lesion of the bony skeleton, but its pathogenesis is unknown.[1] Jaffe and Lichtenstein[2-4] classified the disorder as a congenital anomaly that was the manifestation of malfunctioning bone-forming mesenchyme. Reed,[5] after reviewing 25 cases, attributed the condition to an arrest of bone maturation in the woven stage of development. One (monostotic) or several (polyostotic) bones may be involved. The disorder, which begins as a benign lesion in childhood, is commonly first noticed in adolescence secondary to gross deformity and occasionally pain. The radiographic manifestations vary by site. However, radiolucencies predominate where fibrotic replacement occurs, and a "ground glass" consistency is characteristic of extensive fibro-osseous metaplasia.[2,3] A review of 69 cases by Schlumberger[6] revealed that the most commonly affected sites in descending order were ribs, femur, tibia, maxilla, and calvaria.

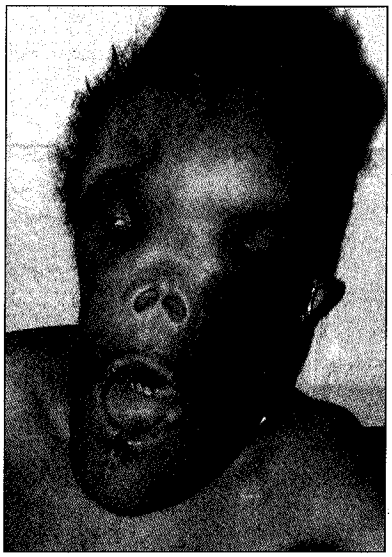

Figure 4. *Postoperative week 2.*

Malignant transformation of fibrous dysplasia was initially described by Coley and Stewart[7] in 1945. Since then, numerous case reports have been published describing transformation in both irradiated and nonirradiated lesions.[8-14] The frequency of malignancy in fibrous dysplasia ranges from 0.5% in monostotic disease to 4.0% in Albright syndrome (polyostotic fibrous dysplasia, hyperpigmented skin macules, and endocrinologic disorders, including isosexual precocity, hyperthyroidism, Cushing syndrome, hyperparathyroidism, and acromegaly).[14-16]

Although sarcomatous transformation in patients with fibrous dysplasia is a rare phenomenon, Schwartz and Alpert[14] noted that the craniofacial region was the most common site of sarcomatous degeneration in polyostotic fibrous dysplasia. In a series of 28 cases reviewed by Ruggieri et al,[10] osteosarcoma was the most common histotype (19), followed by fibrosarcoma (5), chondrosarcoma (3), and malignant fibrohistiocytoma (1). A review of 83 published cases revealed that men and women were affected equally. Fifty-seven percent of the patients had monostotic involvement (vs 43% polyostotic), and a study of the frequency of histologic subtypes found that osteosarcoma was the most common (40 cases), followed by fibrosarcoma (22) and chondrosarcoma (11).[11] Radiation therapy was used as a treatment modality for fibrous dysplasia in only 23 of the cases, suggesting that malignant transformation occurs independent of radiation effects. In concordance with the poor prognosis of advanced-stage sarcoma, the majority of patients in the previous series died of pulmonary metastases, with a mean survival period of 3.4 months.

To our knowledge, this is the first report describing different but simultaneous malignant histotypes (eg, malignant mesenchymoma)[17,18] in fibrous dysplasia (**Figure 5** through **Figure 8**). Ebata et al[9] reported a case of malignant degeneration of fibrous dysplasia of the mandible in which osteosarcoma was found 9 years after a chondrosarcomatous lesion was resected. Despite a stable and predictable disease course in our case, malignant degeneration occurred 25 years after the initial diagnosis. There were no identifiable risk factors, such as a history of prior radiation therapy. Of interest, previous surgical intervention had included 4 debulking procedures of the dysplastic calvaria, bilateral mastoid surgery with canalplasties for external auditory canal stenosis, and placement of ureteral stents for persistent nephrolithiasis.

The sarcomatous transformation in our case has not previously been described, to our knowledge. While cases of osteosarcoma, chondrosarcoma, and fibrosarcoma are rare but well documented, as far as we know no case of a single lesion exhibiting multiple lines

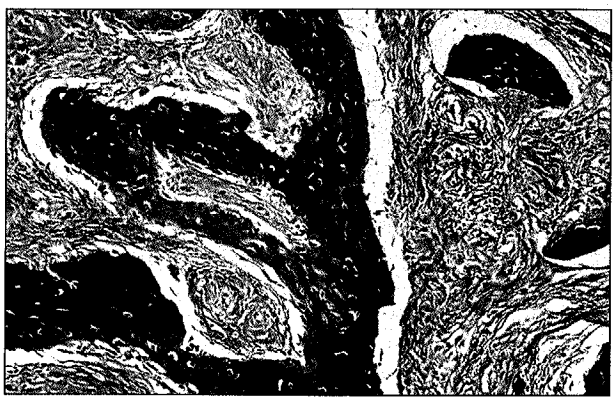

Figure 5. *Irregular bony trabeculae without osteoblastic rimming present in a fibrous background typical of fibrous dysplasia (hematoxylin-eosin, original magnification ×100).*

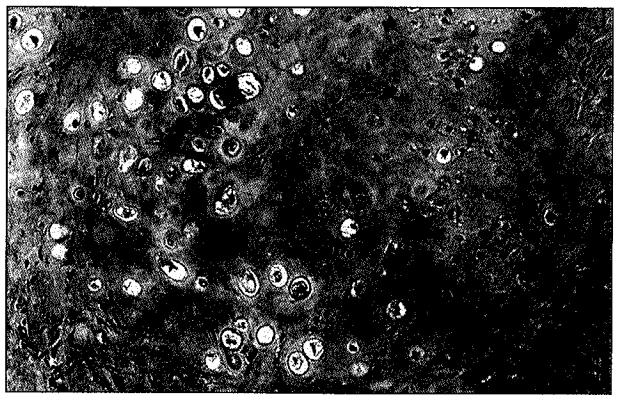

Figure 6. *Area of grade II chondrosarcoma with large atypical chondrocytes occupying lacunae (hematoxylin-eosin, original magnification ×200).*

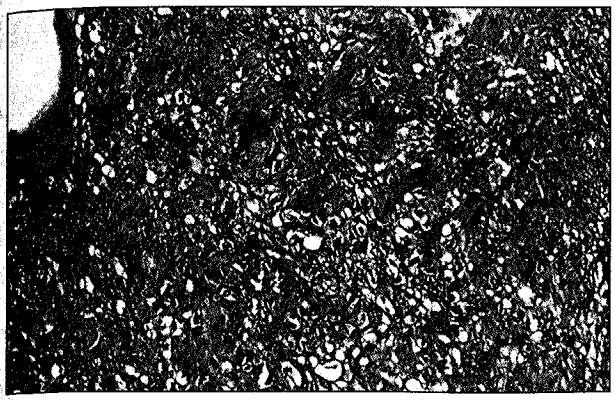

Figure 7. *Photomicrograph illustrating an area showing osteosarcoma differentiation with large atypical osteoblasts separated by "lacy-appearing" osteoid (hematoxylin-eosin, original magnification ×400).*

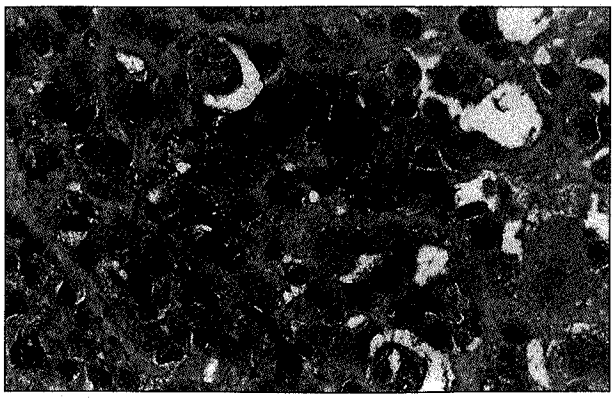

Figure 8. *Poorly differentiated area showing positive immunostaining for muscle-specific actin indicative of rhabdomyosarcoma (anti–smooth muscle antibody immunoperoxidase with hematoxylin counterstain, original magnification ×200).*

of differentiation in a sarcoma arising in the background of fibrous dysplasia has been reported. The tumor in this case clearly showed multiple lines of differentiation with elements of chondrosarcoma, osteosarcoma, and rhabdomyosarcoma. While the exact classification of this neoplasm could be debated, the term *malignant mesenchymoma* appears to be most accurate. This lesion as defined by Stout[19] in 1948 and first described in bone by Schajowicz et al[20] in 1966 is a high-grade sarcoma with 2 or more lines of differentiation other than fibrosarcoma that are apparent either on histological examination or, more recently, on immunohistochemical analysis. It occurs most frequently in the soft tissues, but rare bone lesions have been described. The differential diagnosis of this lesion would include both dedifferentiated chondrosarcoma and chondroblastic osteosarcoma with "other mesenchymal elements." However, if one accepts strict criteria for the former lesion, the high-grade cartilaginous component, as well as the intimate admixture of the different elements without sharp demarcation, makes this diagnosis untenable. While one could argue that the lesion does represent a variant of chondroblastic osteosarcoma, the relative paucity of osteoid-producing tumor, as well as a perfect "fit" for the accepted definition of malignant mesenchymoma, makes us favor the designation *malignant mesenchymoma* for this unusual neoplasm.

Influencing our decision to proceed with surgery was the patient's normal cognitive status as well as his desire for a maximally aggressive therapeutic approach. Our original intent was to perform total excision if possible, add intraoperative radiation therapy and external beam radiation therapy to enhance locoregional control, and then follow with adjuvant chemotherapy for systemic disease. Chemotherapeutic trials with doxorubicin hydrochloride, cisplatin, and pirarubicin have been described in such cases.[9] The aggressiveness of our patient's lesion was characterized by the rapid development of metastatic pulmonary disease within 5 months of resection. A rapidly declining clinical course, including pulmonary metastasis, is consistent with the natural history of malignant mesenchymoma.

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